

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1. (Amended) A method of determining the ability of a *Mycobacterium tuberculosis* bacterium to oxidize ~~a thioamide or a thio carbonyl ethionamide, thiacetazone or thiocarlide~~, said method comprising detecting a mutation in an EtaA gene (SEQ ID NO:1) in said bacterium, which mutated gene encodes an amino acid sequence which differs from that of SEQ ID NO:2 by

~~(a) a frameshift mutation selected from the group consisting of: a deletion at position 65, an addition at position 567, and an addition at position 811, or~~

~~(b) a single nucleotide polymorphism which causes an amino acid substitution selected from the group consisting of: G43C, P51L, D58A, Y84D, T186K, T342K, and A381P, wherein detection of the mutation is indicative of decreased ability to oxidize ~~a thioamide or a thio carbonyl ethionamide, thiacetazone or thiocarlide~~.~~

2. (Canceled)

3. (Original) The method of claim 1, wherein the mutation is a single nucleotide polymorphism which causes an amino acid substitution in an amino acid sequence encoded by said EtaA gene compared to an amino acid sequence of SEQ ID NO:2.

4. (Canceled)

5. (Original) A method of claim 1 wherein the mutation is detected by
(a) amplifying the EtaA gene, or a portion thereof containing the mutation, with a set of primers to provide an amplified product,

(b) sequencing the amplified product to obtain a sequence, and

(c) comparing the sequence of the amplified product with the sequence of a wild-type EtaA gene (SEQ ID NO:1) or portion thereof,

wherein a difference between the sequence of the amplified product and the sequence of the wild-type EtaA gene or portion thereof indicates the presence of a mutation.

6-7. Canceled.

8. (Original) A method of claim 5, wherein said amplification is by polymerase chain reaction.

9. (Original) A method of claim 1, wherein said mutation is detected by hybridizing DNA from said bacterium to a test nucleic acid under stringent conditions.

10. (Original) A method of claim 9, wherein either said DNA from said bacterium or said test nucleic acid is immobilized on a solid support.

11. (Original) A method of claim 1, wherein said mutation is detected by
(a) subjecting said EtaA gene to digestion by restriction enzymes,
(b) separating the resulting restriction products to form a pattern of restriction fragment lengths, and

(c) comparing the pattern of restriction fragment lengths to a pattern of restriction fragment lengths formed by subjecting a known EtaA gene to the same restriction enzymes.

12. (Canceled)

13. (Withdrawn) A method of claim 1, wherein said mutation is detected by specifically binding an antibody to a mutated product of the EtaA gene, wherein the specific binding of the antibody to the mutated gene product is indicative of a mutation which inhibits the ability of the bacterium to oxidize a thioamide.

14. (Withdrawn) A method of claim 13, wherein said gene product is in, or is isolated from, sputum.

15. (Withdrawn) A method of claim 13, wherein detection of said specific binding of said antibody and said mutated gene product is by ELISA.

16. Canceled.

17. (Withdrawn) A method of claim 1, wherein said mutation is detected by
(a) culturing said bacterium in the presence of ethionamide; and
(b) testing for the presence or absence of (2-ethyl-pyridin-4-yl)methanol, wherein the absence of (2-ethyl-pyridin-4-yl)methanol indicates that the bacterium has a mutation which is indicative of decreased ability to oxidize a thioamide.

18 (Withdrawn) A method of claim 17 wherein the presence or absence of (2-ethyl-pyridin-4-yl)methanol is tested by subjecting a medium in which the bacterium is cultured, or the bacterium, to analysis by thin-layer chromatography, high pressure liquid chromatography, or mass spectrometry.

19 (Withdrawn) A method of claim 17, wherein the ethionamide of step (a) is radioactively labeled.

20. (Withdrawn) A method of claim 17, wherein the (2-ethyl-pyridin-4-yl)methanol is radioactively labeled.

21. (Currently amended) A method of screening an individual for a *Mycobacterium tuberculosis* bacterium resistant to treatment by ~~a thioamide or a thiocarbonyl drug ethionamide, thiacetazone or thiocarlide~~, comprising

- (a) obtaining a biological sample containing said bacterium from said individual, and
- (b) detecting a mutation in an EtaA gene (SEQ ID NO:1) in said bacterium, which

mutated gene encodes an amino acid sequence which differs from that of SEQ ID NO:2, wherein said mutation in said EtaA gene is selected from the group consisting of

(i) a frameshift mutation consisting of a deletion at position 65, an addition at position 567, or an addition at position 811, and
(ii) a single nucleotide polymorphism which causes an amino acid substitution selected from the group consisting of: G43C, P51L, D58A, Y84D, T186K, T342K, and A381P, wherein detection of the mutation is indicative said bacterium is resistant to treatment by a thioamide or a thiocarbonyl drug ethionamide, thiacetazone or thiocarlide.

22. (Original) A method of claim 21, wherein the mutation is detected by
(a) amplifying the EtaA gene with a set of primers to provide an amplified product,
(b) sequencing the amplified product to obtain a sequence, and
(c) comparing the sequence of the amplified product with the sequence of a wild-type EtaA gene (SEQ ID NO:1),
wherein a difference between the sequence of the amplified product and the sequence of the wild-type EtaA gene indicates the presence of a mutation.

23-24. Canceled.

25. (Previously presented) A kit for determining the ability of a *Mycobacterium tuberculosis* bacterium to oxidize a thioamide or a thiocarbonyl ethionamide, thiacetazone or thiocarlide, the kit comprising:
(a) a container, and
(b) primers for specifically amplifying an EtaA gene of said bacterium or a portion of said EtaA gene containing a mutation affecting the ability of the bacterium to oxidize a thioamide selected from the group consisting of (i) a frameshift mutation consisting of a deletion at position 65, an addition at position 567, or an addition at position 811, and

(ii) a single nucleotide polymorphism which causes an amino acid substitution selected from the group consisting of: G43C, P51L, D58A, Y84D, T186K, T342K, and A381P.

26-27. Canceled.

28. (Original) A kit of claim 25, further comprising a mutated EtaA gene for use as a positive control.

29. (Canceled)

30. (Withdrawn) A kit for determining the ability of a *Mycobacterium tuberculosis* bacterium to oxidize a thioamide, the kit comprising:

- (a) a container, and
- (b) (2-ethyl-pyridin-4-yl)methanol.

31. (Withdrawn) A kit for determining the ability of a *Mycobacterium tuberculosis* bacterium to oxidize a thioamide, the kit comprising:

- (a) a container, and
- (b) radiolabeled ethioamide.

32. (Withdrawn) A kit for determining the ability of a *Mycobacterium tuberculosis* bacterium to oxidize a thioamide or thiocarbonyl, the kit comprising:

- (a) a container, and
- (b) an antibody which specifically binds to a product of a EtaA gene selected from the group consisting of a wild-type EtaA gene (SEQ ID NO:1) and a mutated EtaA gene.

33. (Withdrawn) A kit for determining the ability of a *Mycobacterium tuberculosis* bacterium to oxidize a thioamide, the kit comprising:

- (a) a container, and
- (b) an antibody which specifically binds to (2-ethyl-pyridin-4-yl)methanol.

34. (Currently amended) A method of determining the ability of a *Mycobacterium tuberculosis* bacterium to oxidize a thioamide or a thiocarbonyl selected from the group consisting of ethionamide, thiacetazone and thiocarlide, said method comprising detecting a mutation in an EtaA gene (SEQ ID NO:1) in said bacterium, which mutated gene encodes an amino acid sequence which differs from that of SEQ ID NO:2, wherein said mutation is selected from the group consisting of

(a) a frameshift mutation consisting of a deletion at position 65, an addition at position 567, or an addition at position 811, and

(b) a single nucleotide polymorphism which causes an amino acid substitution selected from the group consisting of: G43C, P51L, D58A, Y84D, T186K, T342K, and A381P,

wherein detection of the mutation is indicative of decreased ability to oxidize ethionamide, thiacetazone or thiocarlide.

35. (Previously presented) The method of claim 34, wherein the mutation is a frameshift mutation selected from the group consisting of: a deletion at position 65, an addition at position 567, and an addition at position 811.

36. (Canceled)

37. (Currently amended) The method of claim 36 34, wherein the single nucleotide polymorphism causes an amino acid substitution selected from the group consisting of: G43C, P51L, D58A, Y84D, T186K, T342K, and A381P.

38. (Previously presented) A method of claim 34 wherein the mutation is detected by

(a) amplifying the EtaA gene, or a portion thereof containing the mutation, with a set of primers to provide an amplified product,
(b) sequencing the amplified product to obtain a sequence, and

(c) comparing the sequence of the amplified product with the sequence of a wild-type EtaA gene (SEQ ID NO:1) or portion thereof,

wherein a difference between the sequence of the amplified product and the sequence of the wild-type EtaA gene or portion thereof indicates the presence of a mutation.

39. (Previously presented) A method of claim 38, wherein said amplification is by polymerase chain reaction.

40. (Previously presented) A method of claim 34, wherein said mutation is detected by hybridizing DNA from said bacterium to a test nucleic acid under stringent conditions.

41. (Previously presented) A method of claim 40, wherein either said DNA from said bacterium or said test nucleic acid is immobilized on a solid support.

42. (Previously presented) A method of claim 34, wherein said mutation is detected by

(a) subjecting said EtaA gene to digestion by restriction enzymes,
(b) separating the resulting restriction products to form a pattern of restriction fragment lengths, and

(c) comparing the pattern of restriction fragment lengths to a pattern of restriction fragment lengths formed by subjecting a known EtaA gene to the same restriction enzymes.

43. (Canceled)

44. (Currently amended) A method of screening an individual for a *Mycobacterium tuberculosis* bacterium resistant to treatment by a thioamide or a thiocarbonyl drug, selected from the group consisting of ethionamide, thiacetazone and thiocarlide, comprising

(a) obtaining a biological sample containing said bacterium from said individual, and

(b) detecting a mutation in an EtaA gene (SEQ ID NO:1) in said bacterium, wherein said mutation is selected from the group consisting of (a) a frameshift mutation consisting of a deletion at position 65, an addition at position 567, and an addition at position 811, and (b) a single nucleotide polymorphism which causes an amino acid substitution selected from the group consisting of: G43C, P51L, D58A, Y84D, T186K, T342K, and A381P, wherein detection of the mutation is indicative said bacterium is resistant to treatment by ethionamide, thiacetazone or thiocarlide.

45. (Previously presented) A method of claim 44, wherein the mutation is detected by

(a) amplifying the EtaA gene with a set of primers to provide an amplified product,
(b) sequencing the amplified product to obtain a sequence, and
(c) comparing the sequence of the amplified product with the sequence of a wild-type EtaA gene (SEQ ID NO:1),

wherein a difference between the sequence of the amplified product and the sequence of the wild-type EtaA gene indicates the presence of a mutation.

46. (Previously presented) A kit for determining the ability of a *Mycobacterium tuberculosis* bacterium to oxidize a thioamide or a thiocarbonyl selected from the group consisting of ethionamide, thiacetazone and thiocarlide, the kit comprising:

(a) a container, and
(b) primers specific for amplifying an EtaA gene of said bacterium or a portion of said EtaA gene containing a mutation affecting the ability of the bacterium to oxidize ethionamide, thiacetazone or thiocarlide